

REMARKS/ARGUMENTS

The original Claims have been amended in a non-limiting manner to enhance readability. Descriptive support for new Claim 8 is found in Examples 1-3 (isopropanol) on pages 3-5 of the Specification and Example 4 (isoamyl alcohol) on pages 5-6 of the Specification. Descriptive support for new Claim 9 is found in Examples 1, 2 and 4 (anhydrous potassium carbonate) on pages 3-6 of the Specification and Example 3 (anhydrous calcium carbonate) on page 3 of the Specification. Descriptive support for new Claim 10 is found in Example 1, pages 3-4 of the Specification. Descriptive support for new Claim 11 is found in Example 2, page 4 of the Specification. Descriptive support for new Claim 12 is found in Example 3, page 5 of the Specification. Descriptive support for new Claim 13 is found in Example 4, pages 5-6 of the Specification. Descriptive support for new Claim 14 is found on page 3, first full paragraph, of the Specification. Descriptive support for new Claim 15 is found in Example 1 (45 % yield), pages 3-4 of the Specification and Example 4 (41 % yield), pages 5-6 of the Specification. Descriptive support for new Claim 16 is found in Example 2 (2.8 area %) on page 4 of the Specification, Example 1 (1.2-1.5 area %) on pages 3-4 of the Specification, and Example 3 (1.2-1.5 area %) on page 5 of the Specification. No new matter has been entered.

A. The Examiner's rejection

In the Office Action (OA) dated April 18, 2008, the Examiner rejected Claims 1-7 under 35 U.S.C. §103(a) as being unpatentable over Wiedemann (Wiedemann et al., U.S. Patent 4,503,067, issued March 5, 1985).

B. Examiner's claim interpretation

The Examiner first interpreted the scope and content of the method Applicants claim as drawn to (OA, p. 3, para. 3):

. . . a method for preparing Carvedilol, which comprises reacting to 4-(oxirane-2-ylmethoxy)-9H-carbazol with a salt of 2-(2-methoxyphneoxy)-ethylamine [sic, (2-

methoxyphenoxy)] in a specific ratio of the starting materials in the presence of a base in an alcohol solvent.

While the Examiner concluded that the method Applicants claim requires a specific ratio of reactants in the presence of a base and an alcohol solvent in the reaction mixture, the Examiner appears not to have recognized that the “base” in the reaction mixture of the method Applicants claim is the alkali metal or alkaline earth metal carbonate and the alcohol “solvent” in the reaction mixture of the method Applicants claim is a C2 to C5 alcohol.

While we understand that, during the prosecution of an application in the Office, claims are to be given their broadest reasonable interpretation consistent with the teaching in the specification (*In re Bond*, 710 F.2d 831, 833 (Fed. Cir. 1990)), it is error to disregard express limitations in the claims. The Examiner may not set up a “strawman” claim and reject it rather than subject matter encompassed by the actual claims.

The plain language of Applicants’ claims requires “the presence of a base which is an alkali metal or alkaline earth metal carbonate present in an amount of 2.0 to 5.0 equivalents with respect to the starting carbazole, in a solvent selected from the group consisting of C2 to C5 alcohols” (cf Claim 1). The Specification consistently defines the “base” component in the reaction mixture of Applicants’ claimed process as “an alkali metal or alkaline earth metal carbonate” and the alcohol “solvent” as “an alcohol having the number of carbons C2 to C5” (Spec., p. 2, last complete sentence). Applicants submit that the Examiner erred in broadly interpreting the scope and content of the subject matter claimed in a manner inconsistent with the plain language of the claims and the teaching of the Specification.

C. The Examiner’s findings of the scope and content of the prior art

The Examiner found that Wiedemann teaches “a process for preparing Carvedilol which comprises reacting 4-(2,3-epoxypropoxy)carbazol with 2-(2-methoxyphenoxy)-ethylamine in the presence of ethylene glycol dimethyl ether in an alcohol solvent” (OA, p. 4, first para.). The Examiner asks Applicants to “[s]ee the entire reference especially, column 5,

Example 2, and column 6, Example 3.” Applicants have reviewed Wiedemann’s Examples 2 and 3 and reread Wiedemann’s entire disclosure. Applicants fail to understand how the Examiner’s findings with respect to the scope and content of the prior art, whether supported by Wiedemann’s Examples 2 and 3 or any other teaching in the patent, relate to the subject matter Applicants claim and/or would have led a person having ordinary skill in the art to the claimed subject matter. The Examiner has not established that the prior art describes or reasonably would have suggested the presence of a salt of 2-(2-methoxyphenoxy)-ethylamine in the reaction mixture. More specific to the subject matter claimed, the Examiner has not established that the prior art describes or reasonably would have suggested the presence of a salt 2-(2-methoxyphenoxy)-ethylamine in the reaction mixture in the presence of an alkali metal or an alkaline earth metal carbonate base in a C2 to C5 alcohol solvent. The Examiner has not explained when, how, or why Wiedemann’s deficient disclosure reasonably would have taught a person having ordinary skill in the art to employ a salt of the amine reactant itself in a reaction mixture for preparing Carvedilol or in the presence of an alkali metal or alkaline earth metal carbonate base.

Wiedemann does not recognize any stability problems with the amine reactant that Applicants’ invention remedies (see Specification page 2, third para. and page 3, first full para.). Moreover, the Examiner has not pointed to any knowledge or skill in the prior art which would have led a person having ordinary skill in the art to add a carbonate base to a salt of Wiedemann’s amine reactant for any purpose.

The Office has the initial burden of proof to establish the prima facie obviousness of the subject matter Applicants claim in view of the prior art teaching. *In re Fritch*, 972 F.2d 1260, 1265 (Fed. Cir. 1992); *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988). Absent evidence which supports a rejection of the subject matter Applicants claim for obviousness,

the Examiner's conclusion that Applicants' claims are unpatentable under 35 U.S.C. §103(a) must be withdrawn.

D. The Examiner's view of the differences between the prior art and claimed processes

The Examiner finds that "[t]he difference" between Applicants' claimed process and Wiedemann's process is the base" (OA, p. 4, second para., first sentence thereof). The Examiner now states that the "instant process requires the use of an alkali metal or alkaline earth metal carbonate in C₂₋₅ alcohols, whereas Wiedemann teaches the use of ethylene glycol dimethyl ether" (OA, p. 4, second para., second sentence; emphasis added).

First, the Examiner appears to have ignored the fact that the prior art does not describe or reasonably suggest that it is the salt of 2-(2-methoxyphenoxy)-ethylamine which is the reactant present in the reaction mixture of Applicants' claimed process, not the free amine Wiedemann utilizes in its reaction mixtures. Applicants' Specification teaches that the presence of a salt of the amine in the reaction mixture is a significant feature of the claimed invention. As noted above, the Specification teaches (Spec., p. 3, first full para.):

In comparison with other known methods, the method of production of Carvedilol of this invention is more advantageous in that the salt of 2-(2-methoxyphenoxy)ethylamine is used, which is, in comparison with the base, more stable and more available

Second, while the Examiner states that the "instant process requires the use of an alkali metal or alkaline earth metal carbonate in C₂₋₅ alcohols" (OA, p. 4, second para., second sentence), the Examiner ignores the fact that Wiedemann's processes do not describe, disclose, or even suggest the presence of an alkali metal or alkaline earth metal carbonate in its reaction mixtures. The Examiner's findings that (1) Wiedemann uses ethylene glycol dimethyl ether, (2) persons having ordinary skill in the art would have known that the choice of solvent in organic chemistry reaction mixtures is likely to effect the rate of reaction, and (3) Wiedemann contemplates the use of organic solvents at column 4, l. 25 (OA, p. 4, second para., ll. 4-6), do not rectify the defect that Wiedemann does not disclose or reasonably

suggest the presence of a salt of the amine reactant and a carbonate base in the reaction mixture and do not support the Examiner's conclusion that "[t]hus, the current process is considered non-inventive" (OA, p. 4, second para., ll. 6-7).

It is not sufficient for the Examiner to base a rejection for obviousness, as the Examiner has done (OA, pp. 3-4, bridging para.), on the classic patent law axiom that it is within the ordinary skill of the artisan to optimize result effective variables. Persons having ordinary skill in the art would not have acted to optimize the choice or the effect of chemical components Applicants' claims require which the prior art does not disclose and would not have suggested for use in the prior art processes upon which the Examiner relies to make a case for obviousness. Persons having ordinary skill in the art would not have acted to eliminate process problems that the applied prior art does not recognize.

Persons having ordinary skill in the art normally seek "to improve upon what is already generally known." *In re Peterson*, 315 F.3d 1325, 1330 (Fed. Cir. 2003). However, before persons having ordinary skill in the art would want to optimize the choice or use of chemical components in a claimed chemical process, the prior art must at least generally recognize the process and generally suggest the chemical components the claimed process utilizes to achieve its goals. To establish that Applicants' claimed process would have been obvious to a person having ordinary skill in the art, the prior art must reasonably suggest that persons having ordinary skill in the art do what Applicants claims require. Here, the only suggestion to do what Applicants have done is Applicants' own disclosure, i.e. hindsight.

Where, as here, the rejection of the subject matter Applicants claim is based on hindsight, the rejection is improper. *In re Fritch*, 972 F.2d at 1266; *In re Fine*, 837 F.2d at 1075.

E. The Examiner's conclusion of obviousness

The Examiner states that, in light of Wiedemann's teaching, it would have been obvious to a person having ordinary skill in the art to substitute one solvent for another (OA, p. 5, first complete para., ll. 1-2 thereof). The significance of the Examiner's statement can be understood only when it is considered in light of the wealth of clearly erroneous findings which immediately follow it. Consider the statement in context (OA, p. 5, first full para., first sentence):

[O]ne of ordinary skill in the art would be motivated to substitute one solvent for another, in the instance, alkali or alkaline earth metal carbonate as claimed herein for ethylene glycol dimethyl ether since the substitution of the solvents does not affect the outcome of the compound prepared by the process because the same reactants are being used by the current invention and the prior art.

The Examiner's apparent finding that the alkali metal or alkaline earth metal carbonate present in Applicants' reaction mixture is a solvent is clearly erroneous. The Examiner's finding that the alkali metal or alkaline earth metal carbonate present in Applicants' reaction mixture does not affect the outcome of the compound prepared is clearly erroneous. Applicants Specification teaches that the reactants in the claimed process are more stable, the Carvedilol yields are improved, and the contents of the bis-derivative of Carvedilol in the product are lower using Applicants' claimed process relative to the respective stability, yields, and bis-derivative contents of Carvedilol produced by Wiedemann's process (Spec., p. 3, first two full para.). Finally, the Examiner's finding that "the same reactants are being used by the current invention and the prior art" also is clearly erroneous. Applicants' process advantageously utilizes the salt of 2-(2-methoxyphenoxy)-ethylamine, not the unstable 2-(2-methoxyphenoxy)-ethylamine base (Spec., p. 3, first full para., and Examples 1-4).

Conclusions of obviousness based on clearly erroneous findings, as is here the case, cannot stand. *Alza Corp. v. Mylan Labs., Inc.*, 464 F.3d 1286, 1289 (Fed. Cir. 2006).

CONCLUSION

Applicants respectfully submit that the Examiner has not satisfied the Office's initial burden to establish that Claims 1-7 of this application are unpatentable under 35 U.S.C. §103(a). The Examiner appears to have erred in interpreting the scope and content of Applicants' claims, erred in determining the scope and content of the prior art teaching, erred in ascertaining the differences between the prior art and the claimed invention, and based on the accumulated error, erred in concluding that the subject matter Applicants claim is unpatentable under 35 U.S.C. §103(a) for obviousness at the time the invention was made to a person having ordinary skill in the art in view of Wiedemann's disclosure.

For the reasons stated in this amendment and reply to the Office Action dated April 18, 2008, Applicants respectfully request that the Examiner enter new Claims 8-16, withdraw the rejection of Claims 1-7 under 35 U.S.C. §103(a) as being unpatentable over Wiedemann, indicate the allowability of Claims 1-16 (all the claims pending in this application), and pass this case to issue.

Respectfully submitted,

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